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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/734,573	12/12/2003	Wendelin Frick	DEAV2002/0087 US NP	1865

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ANDREA Q. RYAN
SANOFI-AVENTIS U.S. LLC
1041 ROUTE 202-206
MAIL CODE: D303A
BRIDGEWATER, NJ 08807

EXAMINER	
GOON, SCARLETT Y	

ART UNIT	PAPER NUMBER
1623	

NOTIFICATION DATE	DELIVERY MODE
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

USPatent.E-Filing@sanofi-aventis.com
andrea.ryan@sanofi-aventis.com

Office Action Summary	Application No.	Applicant(s)	
	10/734,573	FRICK ET AL.	
	Examiner	Art Unit	
	SCARLETT GOON	1623	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *10 December 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-7 and 9-12* is/are pending in the application.

4a) Of the above claim(s) *9-12* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-7* is/are rejected.

7)☒ Claim(s) *1* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 10 December 2009 has been entered.

DETAILED ACTION

This Office Action is in response to Applicants' Remarks filed on 10 December 2009. No claim amendments were submitted.

Claims 1-7 and 9-12 are currently pending in the instant application. Claim 8 was previously canceled.

Claims 9-12 were previously withdrawn from further consideration in the Office Action dated 4 May 2007 pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention and/or nonelected species, there being no allowable generic or linking claim.

Claims 1-7 will be examined on its merits herein.

Priority

This application claims priority to U.S. provisional application no. 60/466,449 filed on 29 April 2003, German foreign application 10258008.1-43 filed on 12 December

2002, and PCT/EP03/13455 filed on 28 November 2003. A certified copy of foreign priority document 10258008.1-43 in German has been received. An English translation of the German priority document as well as a statement verifying the accuracy of the translation was received by the Office on 22 April 2009.

Claim Objections

Claim 1 is objected to because they include reference characters which are not enclosed within parentheses.

Reference characters corresponding to elements recited in the detailed description of the drawings and used in conjunction with the recitation of the same element or group of elements in the claims should be enclosed within parentheses so as to avoid confusion with other numbers or characters which may appear in the claims. See MPEP § 608.01(m). For example, "formula I" should be written as "formula (I)".

Appropriate correction is required.

The following are new grounds of rejection.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).
A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this

application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.
Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer.
A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1-7 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-13 of U.S. Patent No. 7,288,528 B2.

Although the conflicting claims are not identical, they are not patentably distinct from each other because the patent is drawn to compounds of formula (I), (Ia) and (1b), as well as a method of treating type 1 or type 2 diabetes and a method of lowering blood glucose which comprises administering to a subject in need thereof a therapeutically effective amount of a compound of formula (I). The claims are drawn to a compound of formula (Ib), which is a sub-genus of the compounds of formula (I), wherein R1 is F and R2 is H; R1 is H and R2 is F; or R1 is F and R2 is F; R3 is OH, A is O, R4 is hydrogen, methyl, methoxy, or OH; R5 is hydrogen, F or methoxy; B is $-CH_2-$, $-CO-NH-CH_2-$, -O- or $-CO-CH_2-CH_2-$, Cyc1 is phenyl; R7 is hydrogen; R8 is hydrogen, OH, ethyl, Cl, OCF_3 or methoxy; R9 is hydrogen; or R8 and R9 taken together form $-CH=CH-O-$ or $-CH_2-CH_2-O-$, and, with the carbon atoms in which they are attached form a 5-membered ring.

The claims of the instant application are drawn to a compound of formula (I) with the limitations for each variable as indicated in the claims. Many, if not all, of the substituents for each variable are the same as that in U.S. Patent No. 7,288,528 B2.

Thus, the instant claims 1-7 are seen to be anticipated by claims 1-13 of U.S. Patent No. 7,288,528 B2.

Claims 1-7 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-13 of copending application no. 11/926,697.

Although the conflicting claims are not identical, they are not patentably distinct from each other because the copending application is drawn to compounds of formula (I), (Ia) and (1b), as well as a method of treating type 1 or type 2 diabetes or a method of lowering blood glucose which comprises administering to a subject in need thereof a therapeutically effective amount of a compound of formula (I). The claims are drawn to a compound of formula (Ib), which is a sub-genus of the compounds of formula (I), wherein R1 is F and R2 is H; R1 is H and R2 is F; or R1 is F and R2 is F; R3 is OH, A is O, R4 is hydrogen, methyl, methoxy, or OH; R5 is hydrogen, F or methoxy; B is $-CH_2-$, $-CO-NH-CH_2-$, -O- or $-CO-CH_2-CH_2-$, Cyc1 is phenyl; R7 is hydrogen; R8 is hydrogen, OH, ethyl, Cl, OCF_3 or methoxy; R9 is hydrogen; or R8 and R9 taken together form $–CH=CH-O-$ or $–CH_2-CH_2-O-$, and, with the carbon atoms in which they are attached form a 5-membered ring.

The claims of the instant application are drawn to a compound of formula (I) with the limitations for each variable as indicated in the claims. Many, if not all, of the substituents for each variable are the same as that in copending application.

Thus, the instant claims 1-7 are seen to be anticipated by claims 1-13 of copending application no. 11/926,697.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

The following rejections of record in the previous Office Action are maintained.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-7 are rejected under 35 U.S.C. 103(a) as being unpatentable over WIPO publication WO 2002/036602 to Ohsumi *et al.* (IDS dated 5 March 2004; U.S. Patent No. 6,815,428 B2 used as English equivalent), in view of journal publication by Díez-Sampedro *et al.* (of record).

Ohsumi *et al.* teach pyrazole-O-glycoside derivatives represented by formulas (1A) and (1B) for use as a diabetic medicine (abstract; column 1, lines 55-67; column 2, lines 1-14; claim 1). Exemplary compounds 1-16 are also shown (columns 31-35). Pharmaceutical compositions comprising the aforementioned compounds inhibit the Na^+-dependent glucose transporter (SGLT), which reduces renal glucose reabsorption at renal uriniferous tubules (column 1, lines 15-18 and lines 37-40). As a result, the

level of blood sugar decreases. SGLT-1 and SGLT-2 are known membrane proteins which transport glucose.

Ohsumi *et al.* do not teach pyrazole-O-glycoside derivatives wherein the C-4 hydroxyl is substituted with a fluorine atom.

Díez-Sampedro *et al.* teach the effects of varying the hydroxyl groups on the glucose ring and its recognition by the Na^+-dependent glucose transporter (SGLT1). SGLT1 is highly selective for its natural substrates, D-glucose and D-galactose (abstract). Díez-Sampedro *et al.* individually substituted the different hydroxyl groups on the glucose ring with a hydrogen, fluorine or methyl group and studied the ability of SGLT1 in recognizing and binding the modified substrate (p. 49189, column 1, subsection "Compounds"; p. 49189, column 2, full paragraphs 3-5). The only increase in the apparent affinity, compared with glucose, was found when the equatorial hydroxyl group in the fourth position was replaced with a fluorine atom (4F4DOglc) where the $K_{0.5}$=0.07mM (p. 49189, column 2, fifth full paragraph). Since 4F4DOglc had a lower $K_{0.5}$ compared with glucose (six times higher affinity), Díez-Sampedro *et al.* concluded that the hydrogen bond donation of the fourth position of glucose was detrimental to sugar binding (p. 49192, column 1, third full paragraph).

It would have been obvious to one of ordinary skill in the art at the time of the invention to combine the teachings of Ohsumi *et al.* patent, regarding pyrazole-O-glycoside derivatives that inhibit the Na^+-dependent glucose transporter (SGLT) for use as a diabetic medicine, with the teachings of Díez-Sampedro *et al.*, regarding the increased apparent affinity of 4F4DOglc by SGLT as compared with the native glucose

substrate. One would have been motivated to combine the teachings and substitute the 4-OH group of the pyrazole O-glycoside compounds taught by Ohsumi *et al.*, with a fluorine atome, in order to receive the expected benefit, as suggested by Díez-Sampedro *et al.*, that SGLT has a higher apparent affinity for the glucose substrate when the 4-hydroxyl group is replaced with a fluorine atom. A medicinal chemist would view that a compound with an increased apparent affinity for a receptor, as in the situation described by Díez-Sampedro *et al.*, can likely serve as an inhibitor of the substrate, and would thus have been motivated to synthesize such a compound as inhibitors of SGLT can be used as a diabetic medicine.

Thus, the claimed invention as a whole is *prima facie* obvious over the combined teachings of the prior art.

Response to Arguments

Applicants' arguments, filed 10 December 2009 with respect to the rejection of claims 1-7 made under 35 USC § 103(a) as being unpatentable over Ohsumi *et al.* in view of Díez-Sampedro *et al.*, have been fully considered but they are not persuasive.

Applicants argue that the Díez-Sampedro *et al.* reference represents a "teaching away" inasmuch as it was known in the art (e.g. Ellsworth *et al.* of WO 01/27128) that inhibition of SGLT-1 is undesirable due to predicted severe side effects. Applicants further argue that there is no requirement that a reference *definitively* teach anything in order to constitute as "teaching away" from the invention, rather, that a prior art reference that diverges and points in a technical direction away from the present

invention is evidence that the invention is unobvious. Applicants further state that "a reference will teach away when it suggests that the developments flowing from its disclosures are unlikely to produce the objective of the applicant's invention," citing *In re Gurley*, 27 F.3d 551, 553 (Fed. Cir. 1994).

These arguments are not persuasive because, contrary to Applicants' arguments, the disclosure of Ellsworth *et al.* that "[i]nhibition of SGLT1 could also have serious adverse consequences," does not constitute a "teaching away" from the claimed invention "because such disclosure does not criticize, discredit, or otherwise discourage the solution claimed" *In re Fulton*, 391 F.3d 1195, 1201, 73 USPQ2d 1141, 1146 (Fed. Cir. 2004). Applicants are requested to note that there are numerous known drugs that are known to have serious adverse consequences. For example, it has been shown that antidepressants increase the risk of suicidal thinking and behavior in children, adolescents, and young adults, as compared to placebo. However, these drugs are still administered because the practitioner considers the benefits to outweigh the serious adverse consequences. Thus, the suggestion that a drug may have serious adverse consequences would not necessarily discourage one of ordinary skill in the art from arriving at the claimed invention, particularly if the outcome is considered to be beneficial. Moreover, in the instant situation, the combined teachings of the prior suggest one of ordinary skill in the art to only substitute the C-4 hydroxyl group of the glycosyl residue with a fluorine atom. Thus, under the current legal standard for obviousness (*KSR*, 550 U.S. at___, 82 USPQ2d at 1396), since there is a finite number of compounds to try, namely, one, it would have been *prima facie* obvious for one of

ordinary skill in the art to try making such a compound, with the expectation that it would result in a compound that functions as an SGLT-1 inhibitor. The rationale to support a conclusion that the claim would have been obvious is that "a person of ordinary skill has good reason to pursue the known options within his or her technical grasp. If this leads to the anticipated success, it is likely that product [was] not of innovation but of ordinary skill and common sense. In that instance the fact that a combination was obvious to try might show that it was obvious under § 103." KSR, 550 U.S. at ___, 82 USPQ2d at 1397. See also MPEP § 2143.

The rejection is still deemed proper and therefore adhered to.

Conclusion

In view of the rejections to the pending claims set forth above, no claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to SCARLETT GOON whose telephone number is 571-270-5241. The examiner can normally be reached on Mon - Thu 7:00 am - 4 pm and every other Fri 7:00 am - 12 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Shaojia Jiang can be reached on 571-272-0627. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Shaojia Anna Jiang/
Supervisory Patent Examiner, Art Unit 1623

SCARLETT GOON
Examiner
Art Unit 1623